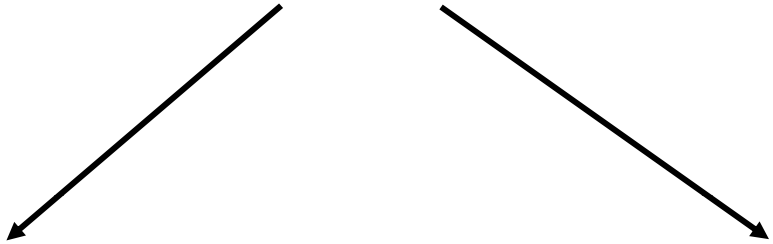
Discover variant(s) that alter risk

(+ Environmental Factors)



Prevention

Counseling

- **Life Style**
- **Diet**

Surveillance

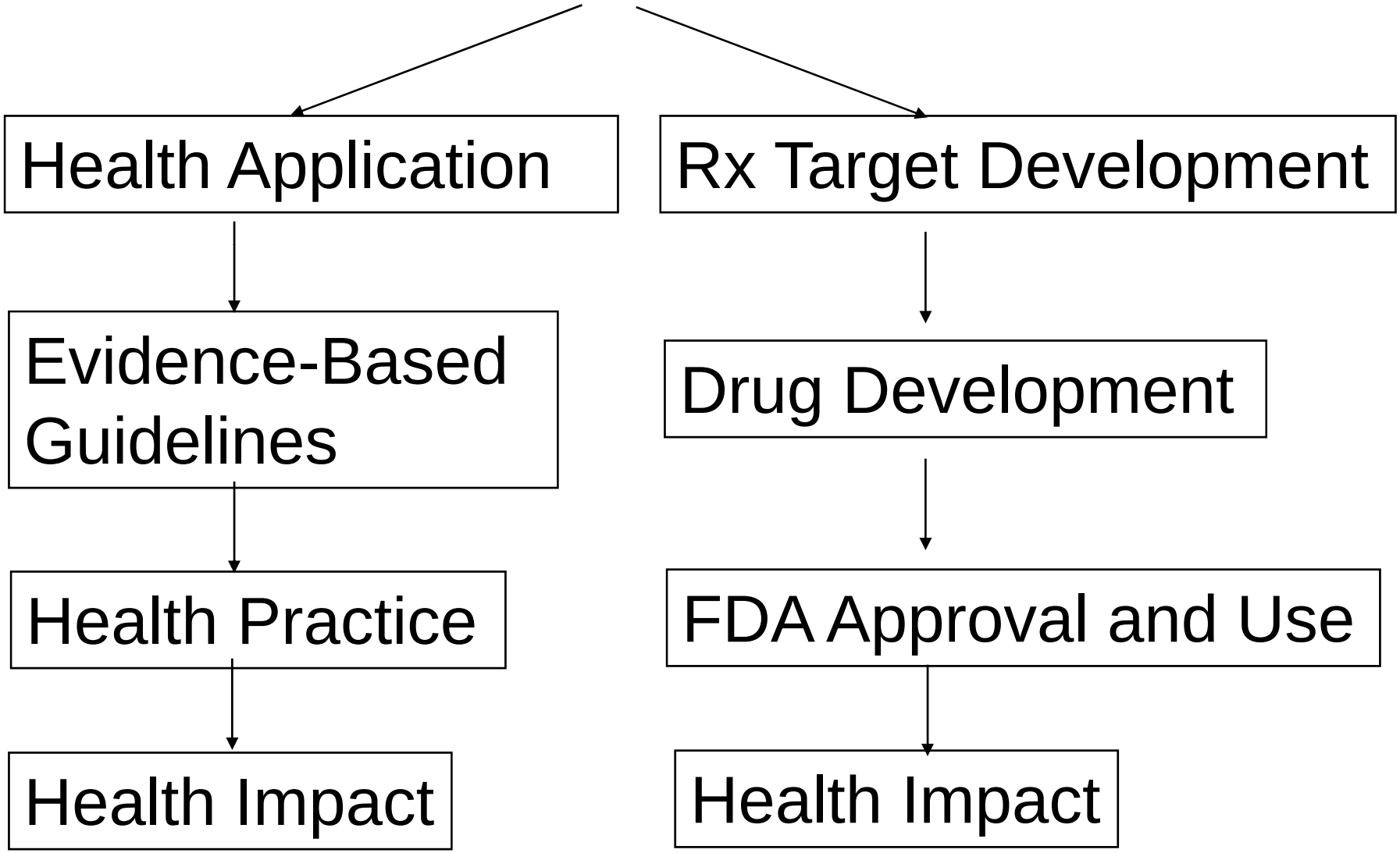
Treatment

Drugs

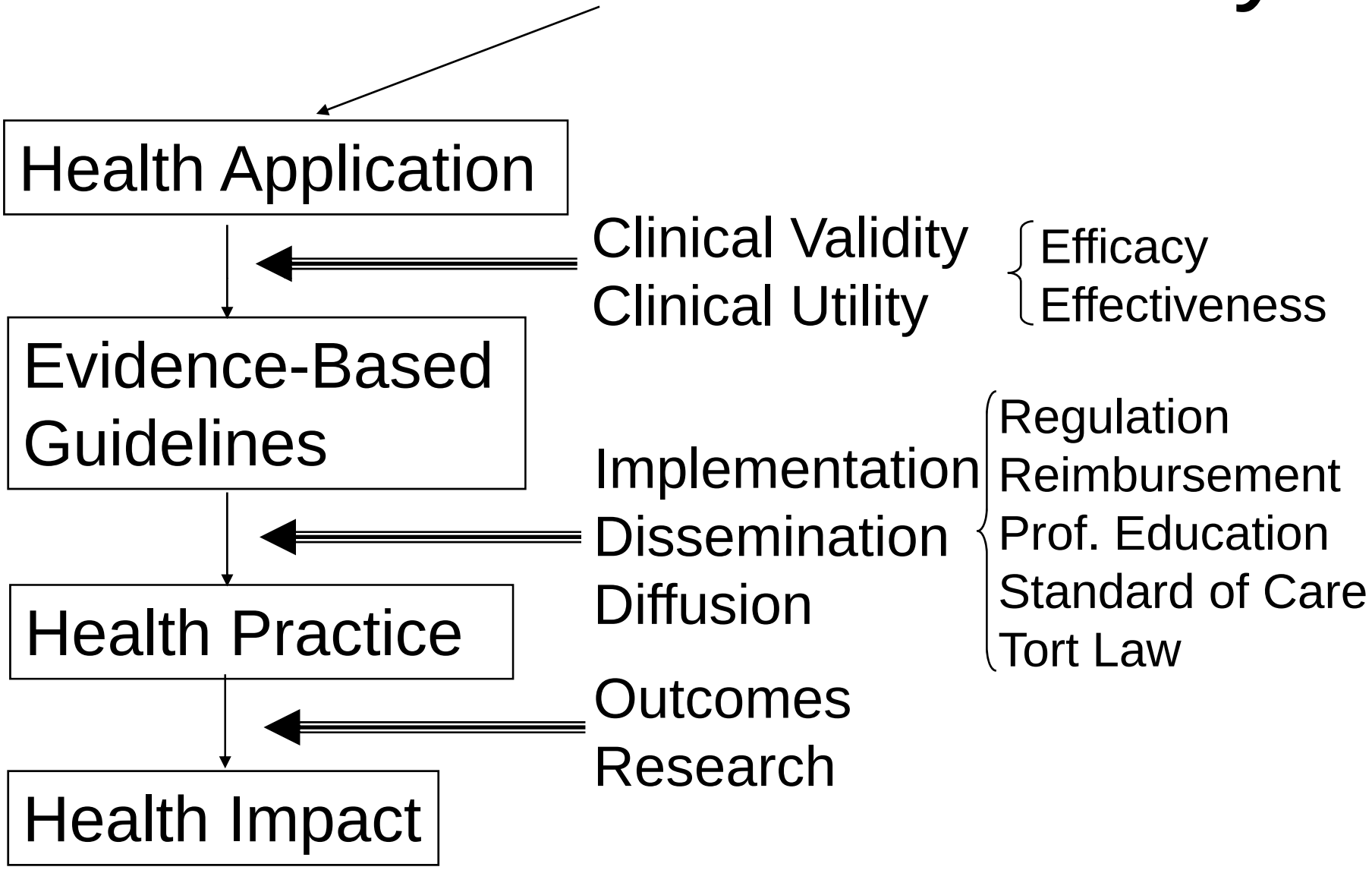
Rx Stratification

Avoid Adverse Events

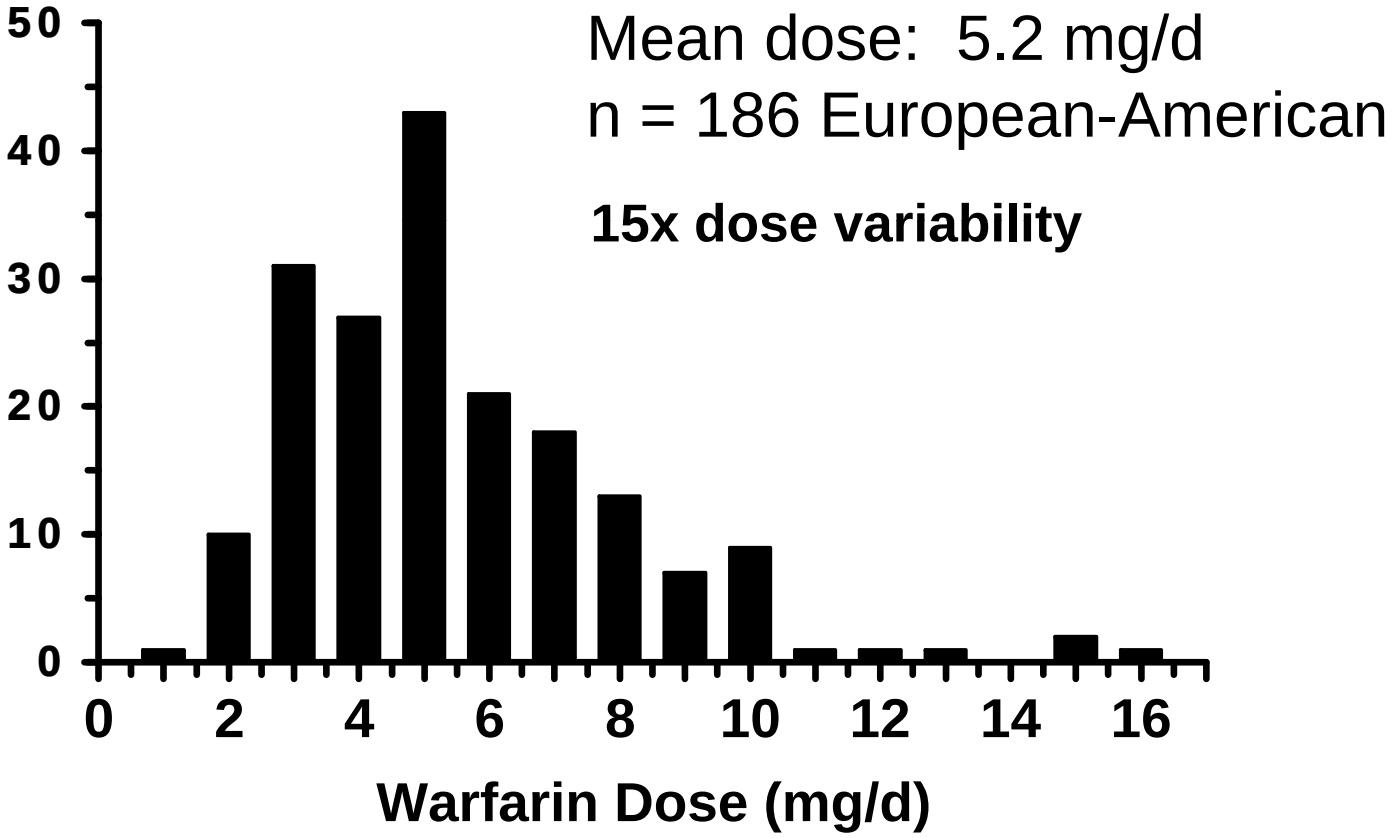
Gene & Variant Discovery



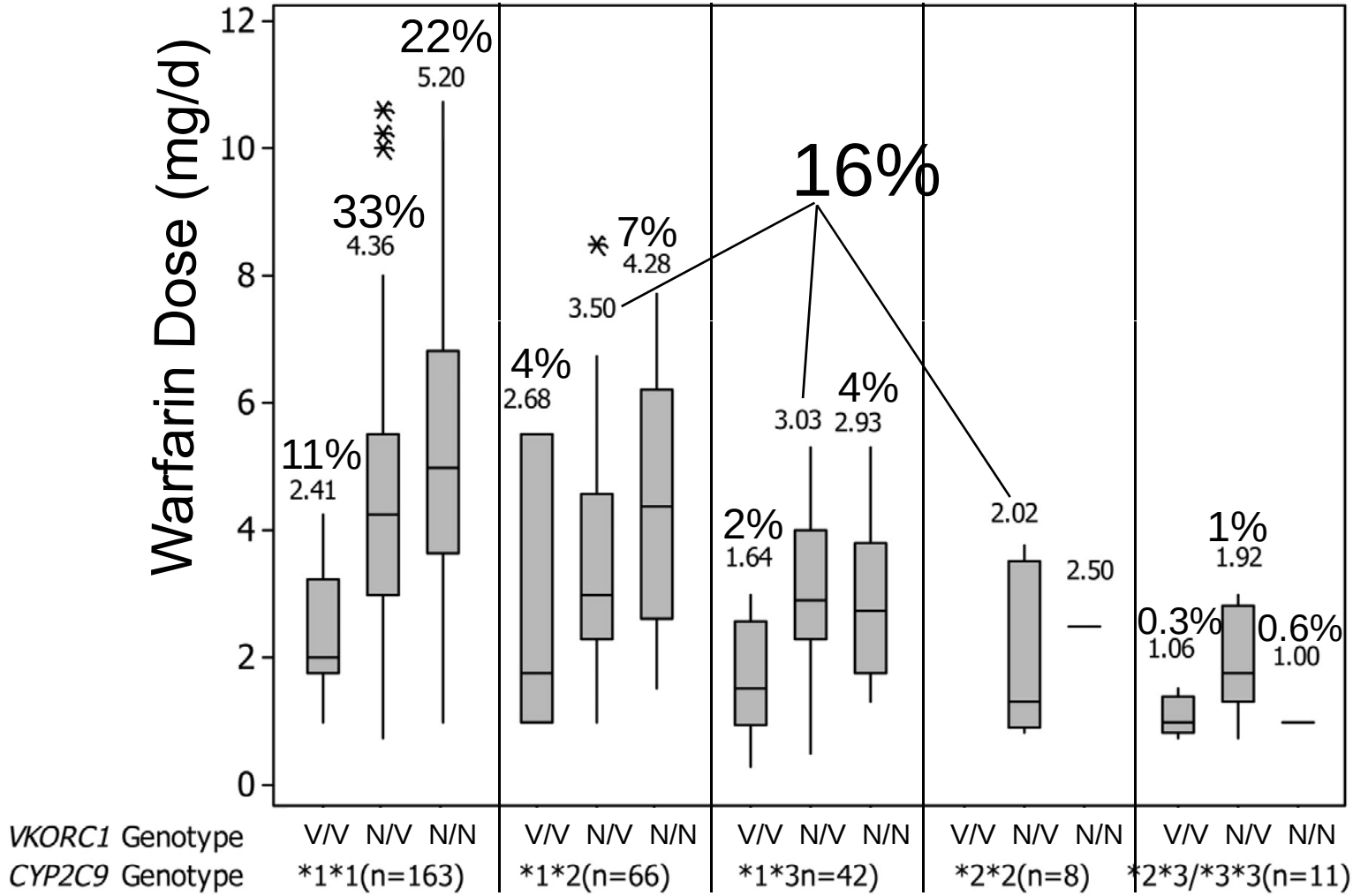
Gene & Variant Discovery



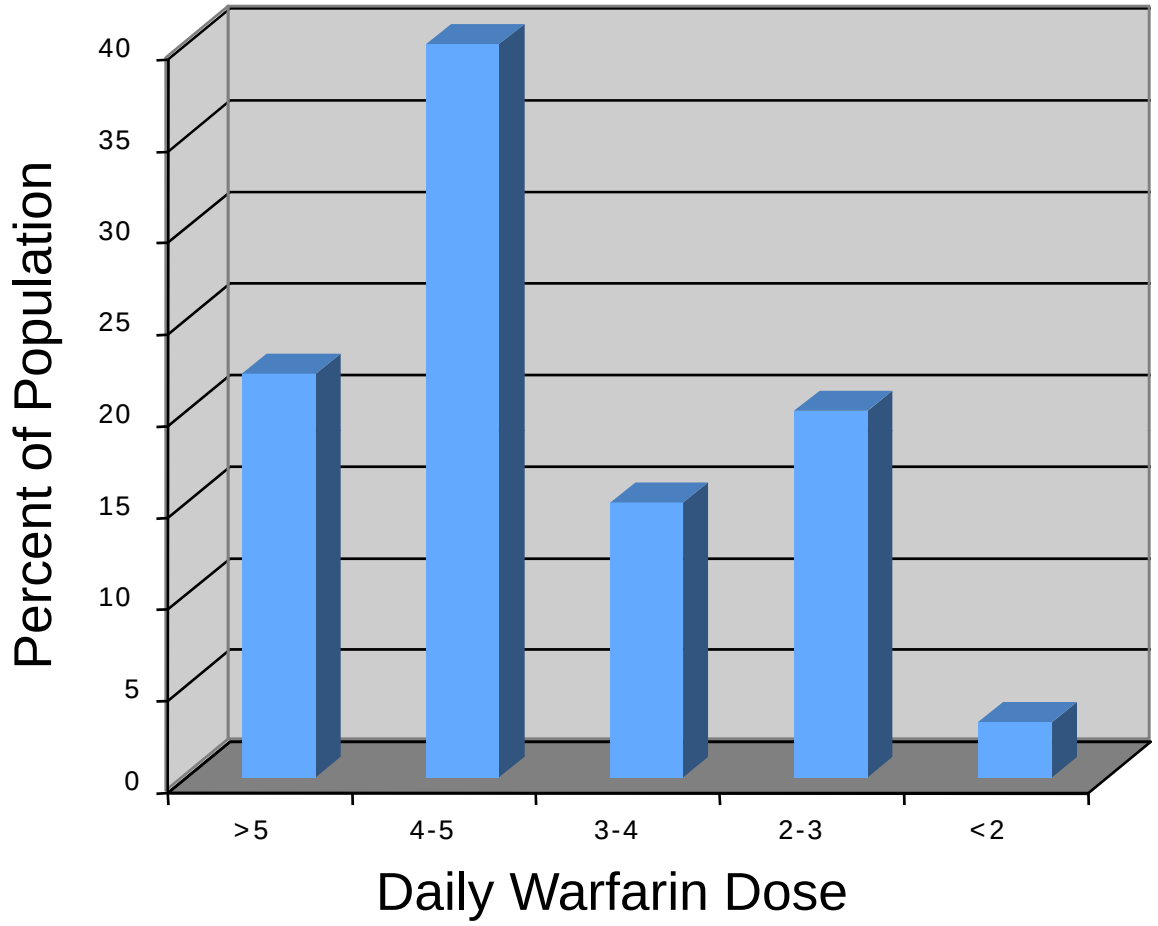
Warfarin -Variable Dose Requirement



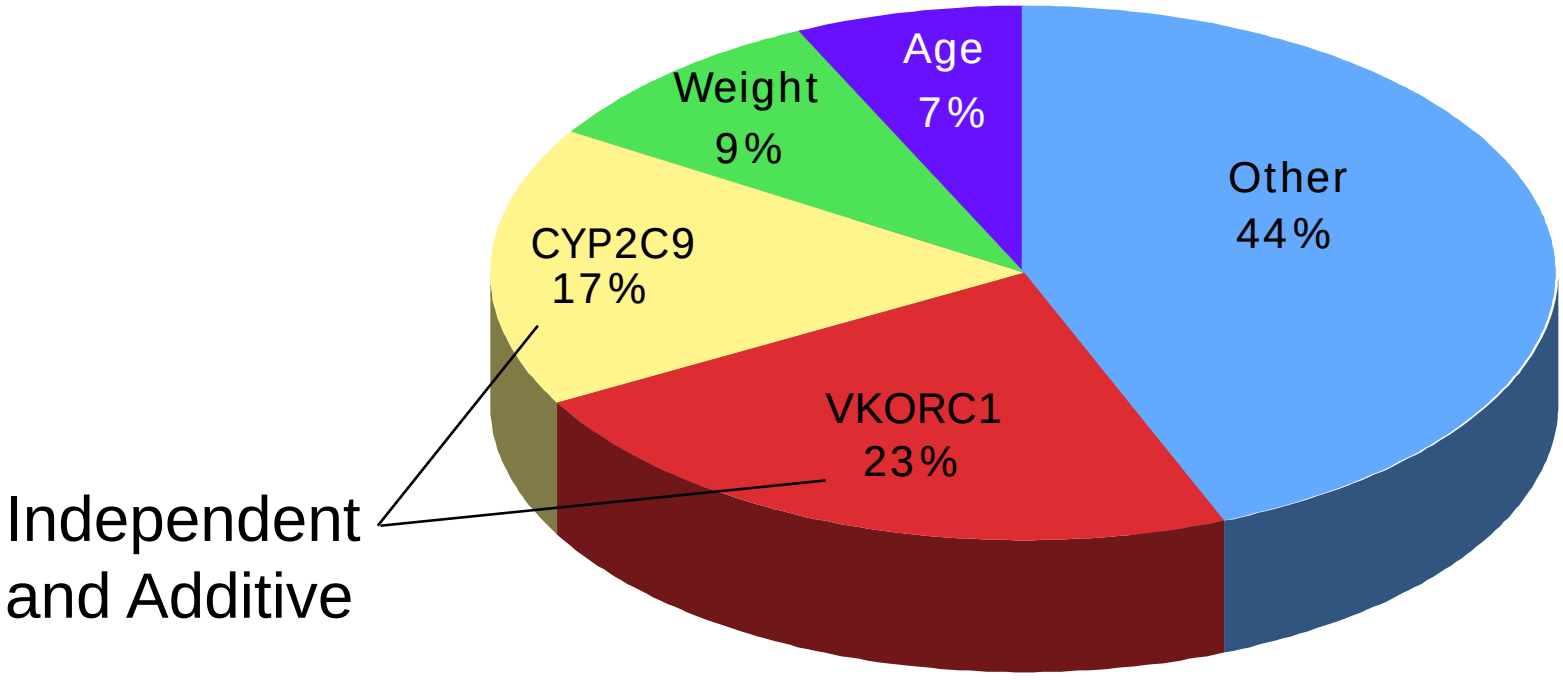
Clinical Validity of *CYP2C9* and *VKORC1* genotype on warfarin dosage



Sconce, E. A. et al. Blood 2005;106:2329-2333

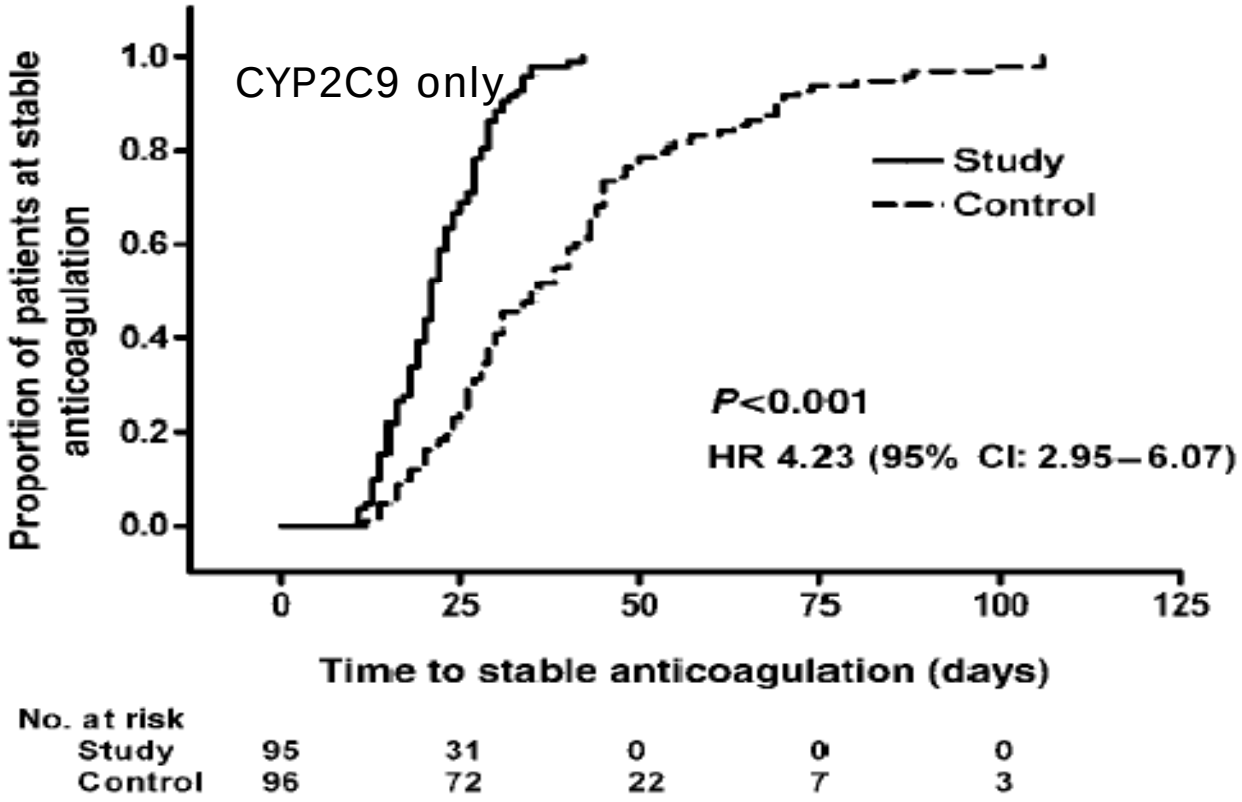

Percent of Population
40
35
30
25
20
15
10
5
0
>5
4-5
3-4
2-3
<2
Daily Warfarin Dose

Sources of Variability in Warfarin dose at stable INR



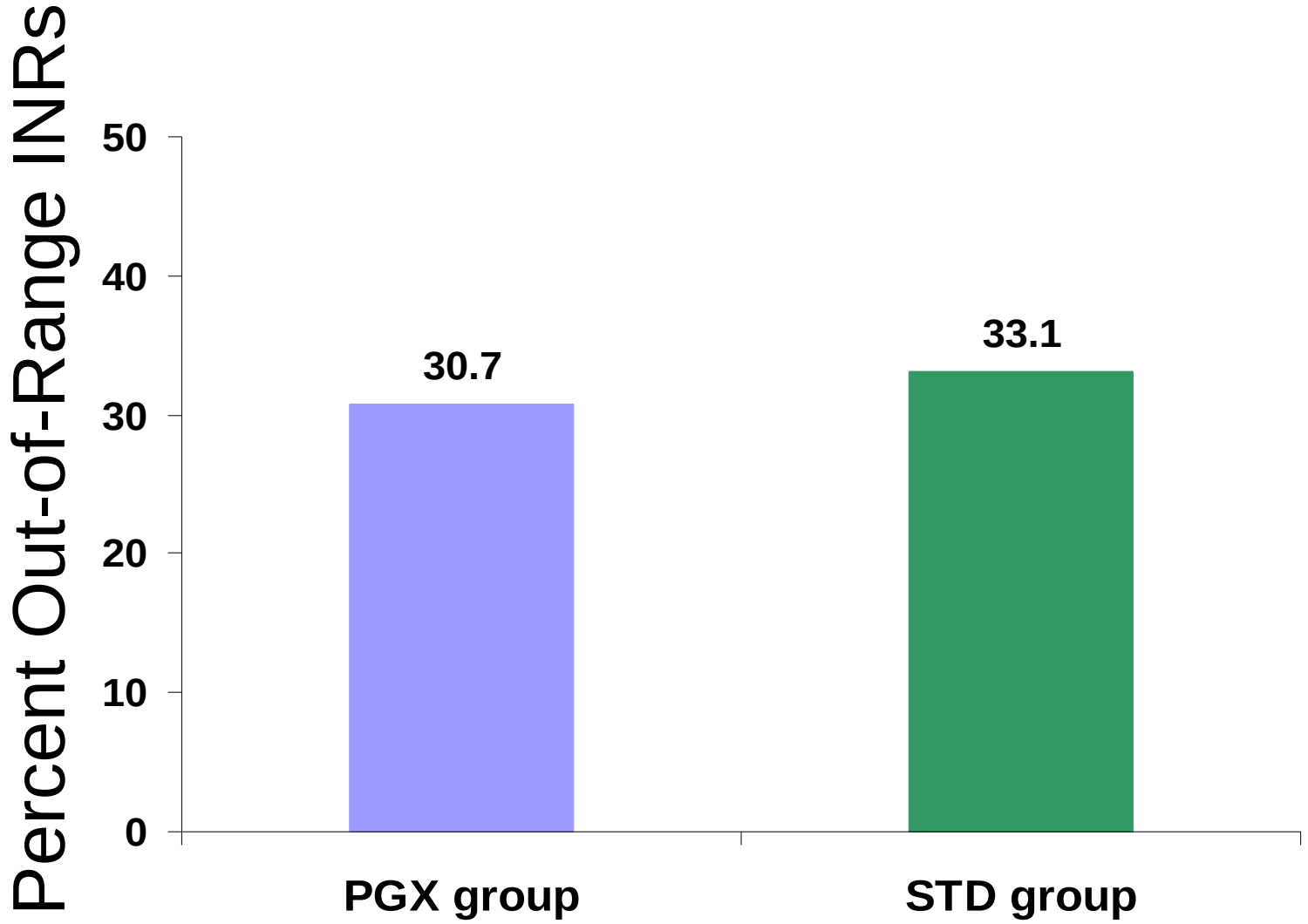
Time to Stable Anticoagulation

Israeli Prospective Study



Clin. Pharmacol. Ther 2007; Sept. Epub

Couma-Gen Study



Circulation 2007;116:epub

Implementation Dissemination Diffusion

2,000,00 new warfarin prescriptions per year
= $300-400 Million per year in testing

To paraphrase a Blue Cross/Blue Shield Technology Assessment Committee member:

“Spending more $ and getting no benefit is ‘bad buy’.

The Problem is how to deal with incremental improvements to outcome that come with cost, I.e. cost effectiveness. Can you afford everything that is a “good buy?”

Business Weekly

Genzyme Genetics and Third Wave Technologies Inc. establish a preferred marketing relationship to provide testing with the Invader® UGT1A1 Molecular Assay for colorectal cancer patients in the North American market who are being considered for, or currently taking, the chemotherapy Camptosar® (irinotecan).

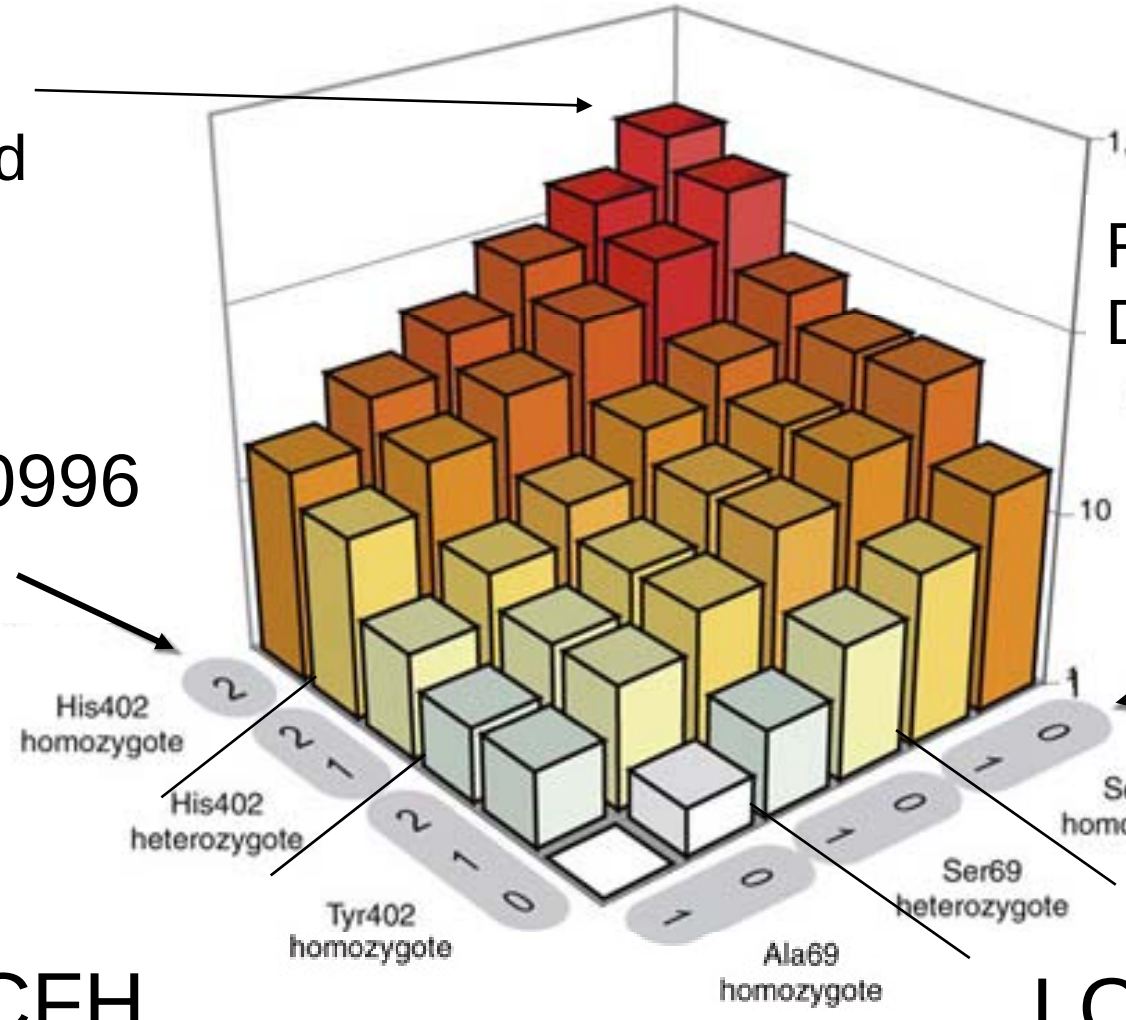
Genzyme Corporation enters a licensing agreement with the Mass General (MGH) and Dana-Farber Cancer Institute (DFCI) for exclusive, worldwide diagnostic rights to gene mutations in the EGFR gene. Genzyme will develop and market a diagnostic test to help identify patients with non-small cell lung cancer who are most likely to respond to targeted lung cancer therapies, including Tarceva(TM) (erlotinib) and Iressa(R) (gefitinib).

Financial Results with both tests are disappointing…why? Two different reasons

Is it important for a patient to know whether he has the *TCF7L2* gene variant?

	Freq	PPV	NPV
+/V	0.40	7.5%	95%
V/V	0.07	13%	95%

280-fold increased



Relative Disease Risk

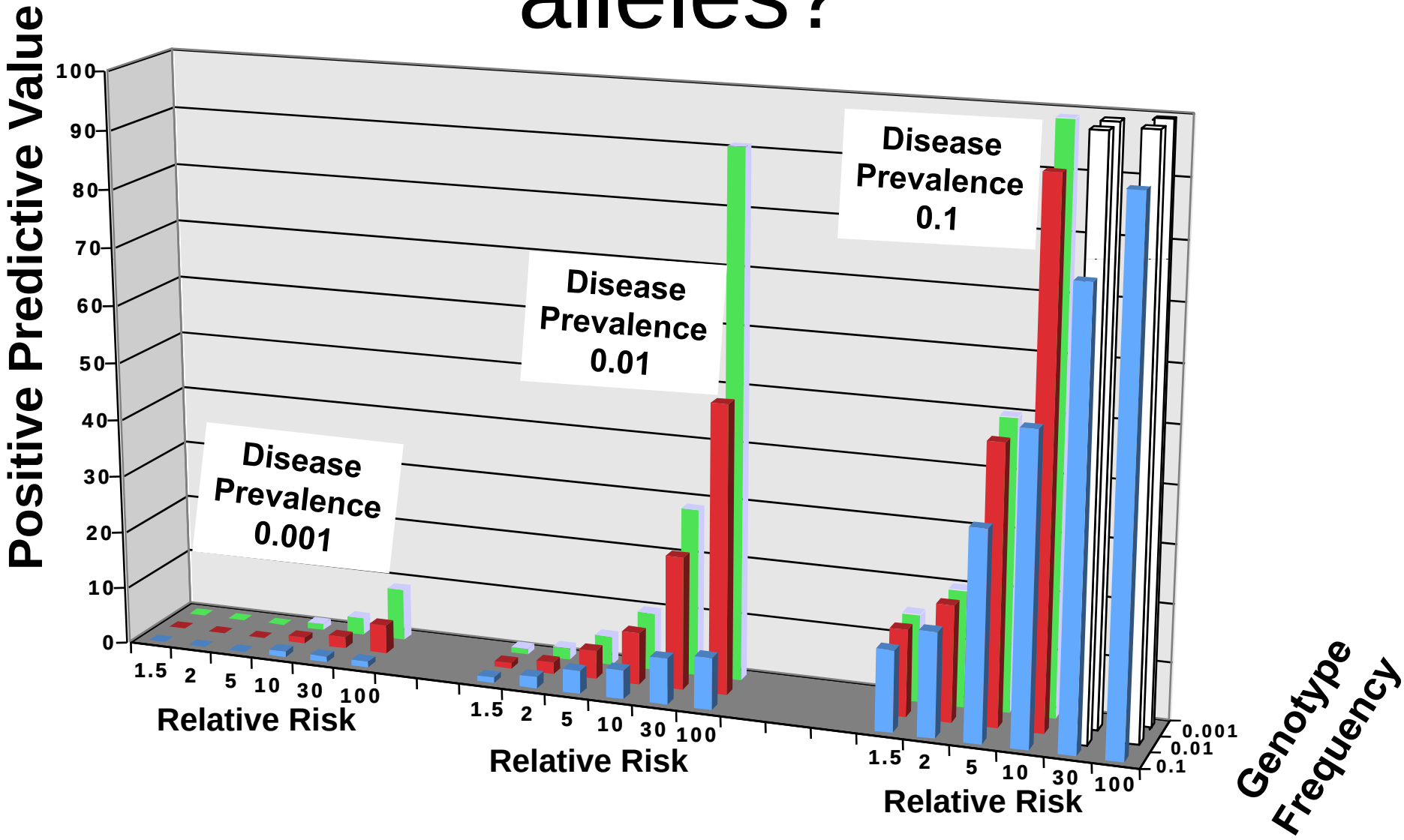
rs1410996 alleles

C2-CFB

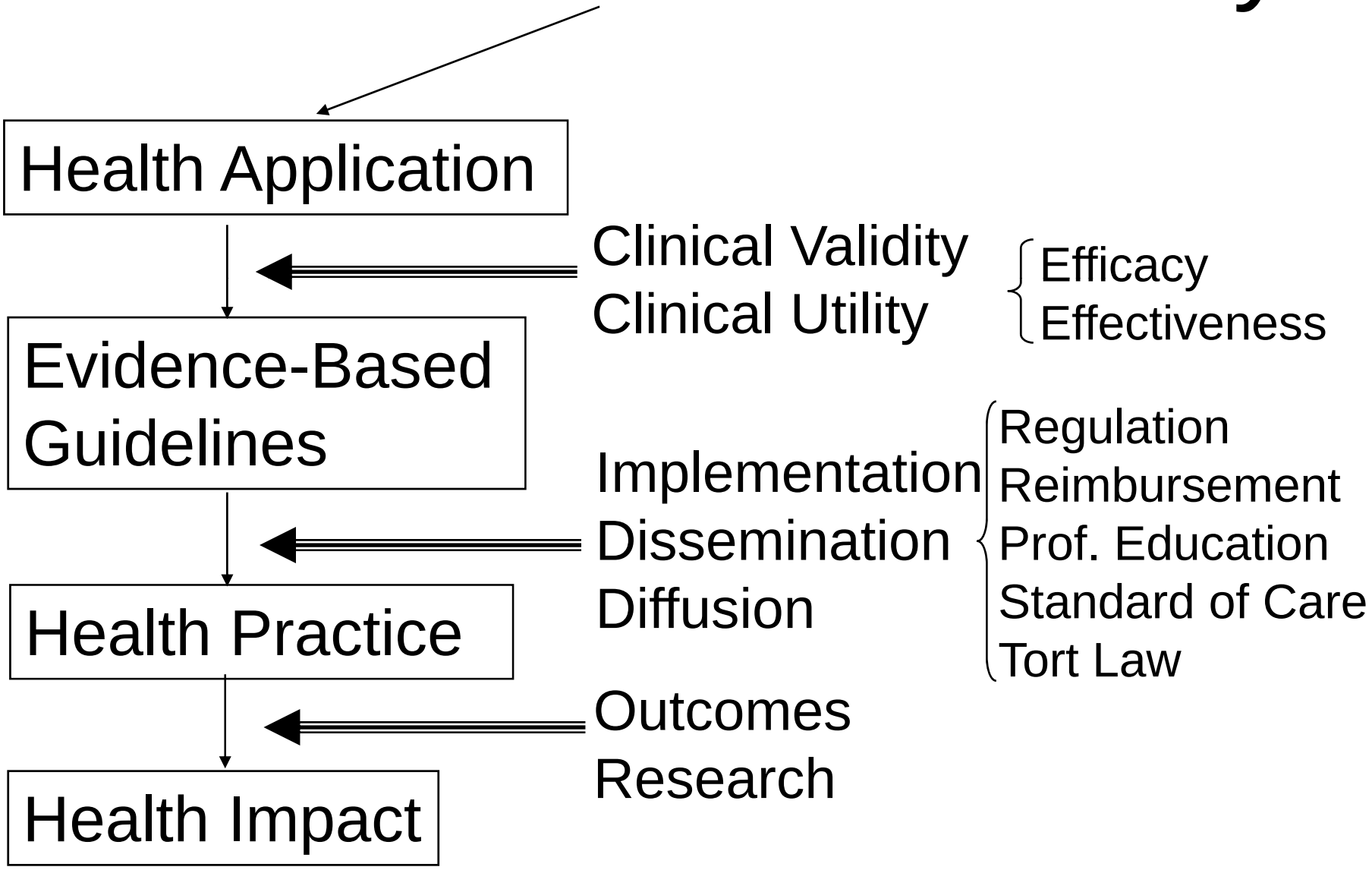
CFH

LOC387715

Can we combine multiple risk alleles?



Gene & Variant Discovery



Recommendations

1. Keep the Gene Variants Coming
2. Provide the **Functional** Tools to Support Clinical Validity Studies
3. Inform/Motivate other NIH ICs, CDC, CMS, BC/BS, AHRQ to fund Clinical Utility Studies
4. NIH consensus Conferences on use of variants in Clinical Medicine
5. Journalist and Science Writer Education
6. Training Clinical Pharmacists in Genetics to serve as test translators